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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,654	12/17/2001	Frank W.R. Chaplen	245-61614	3259

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KLARQUIST SPARKMAN, LLP
One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, OR 97204

EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,654	CHAPLEN ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11,13,25 and 27-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-11,13,25,27-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed September 25, 2003 has been received and entered into the case. Claims 2, 12, 14 – 24 and 26 are canceled and claims 28 – 30 are added. Claims 1, 3 – 11, 13, 25 and 27 – 39 are pending and have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 28 – 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification as originally filed, in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, while the specification teaches chromatophores entrapped into beads that are then encapsulated with polymers, the specification fails to teach any cartridge or sealed container comprising chromatophores. Therefore, the limitations are rendered matter which was not described in the specification as originally filed.

3. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is rendered vague and indefinite because it is unclear how a bead is a capsule. Applicant fails to define the term capsule to include a bead, so it is unclear how the plain meaning of "capsule" would include a bead.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Elving or Lerner.

Applicant claims a method for detecting a bioactive compound, the method comprising exposing isolated chromatophores to a bioactive compound or organism and quantifying an optical change in at least one chromatophores in response to the bioactive compound.

Elving teaches a method for detecting a pertussis toxin (bioactive compound), comprising exposing chromatophores (chromatophores isolated from fish) to a sample (compound), and observing for changes in color (abstract).

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67).

The references anticipate the claimed subject matter.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 3 – 9, 11, 13, 25, 27 – 29 and 33 – 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elving and/or Lerner.

Applicant newly claims a method for detecting bioactive compounds or organisms, the method comprising providing a capsule comprising chromatophores, introducing a bioactive compound/organism into the capsule, and detecting a change in at least one chromatophores in response to the compound/organism. The chromatophores are fish; the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from a neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators, caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins; the organism is a bacteria, fungus, virus, plant or animal; and the chromatophores are Betta chromatophores. The method further comprises exposing a first type of chromatophore to the compound, exposing a second type of chromatophore to the compound, and identifying a class of compounds based on the detected response of the chromatophores, wherein the first and second chromatophores are fish melanophores and erythrophores. The method further comprises detecting a color change from a first color prior to contact and to a second color after contact to the compound. Alternatively, the method comprises selecting a bacteria which produces an induced response on the chromatophore, exposing the chromatophore-bacteria combination to the compound, exposing the chromatophore-cell combination to a control compound, measuring the response of the chromatophore to the control, evaluating the compound based on the cell induced response, the measured response, and the control response; wherein the test cell is a

bacteria associated with a cell induced response which inhibits a chromatophore response and the control is norepinephrine. Finally, the detection of optical change is computer aided.

Elving teaches a method for detecting a pertussis toxin (bioactive compound), comprising exposing toxin sensitive fish chromatophores to a sample (compound), and observing for changes in color (abstract). Specifically, the method includes observing for pigment aggregation and hue changes (col.2 line 36-40). Fish chromatophores are exposed compounds that aggregate pigments, then to samples of body fluid (which contain bacterium) wherein the toxin inhibits pigment aggregation (or the chromatophore response), and is observed for color changes (col.2 line 36-46). Melanophores are used because they provide distinct and rapid color change (col.3 line 1-3) and noradrenaline (norepinephrine) is used as the control (col.3 line 65 – col.4 line 5).

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a control compound that disperses/aggregates pigments within the melanophores; followed by exposure to the bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67). Lerner teaches that the pigment cells may be chromatophores, melanophores, or erythrophores (col.3 line 18-21) obtainable from Pisces, or fish (coll3 line 23-26).

The references do not specifically teach the chromatophores in capsules. However, Elving and Lerner both teach kits wherein the various components are in containers (or capsules) before use. Specifically, Elving teaches separately packaged chromatophores (col.3 line 35 – 47) and Lerner teaches containers with the chromatophores (col.7 – 9). Furthermore, as the references use titer wells, one of ordinary skill in the art would have known to use caps on such

plates as a matter of routine aseptic laboratory practice. Thus, the capped wells would have acted as a capsule comprising chromatophores.

The references do not teach the method wherein both erythrophores and melanophores are used together. However, Lerner specifically teaches that melanophores and/or erythrophores may be used in the methods. At the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use either or both of the named chromatophores in the methods of Lerner and/or Elving with a reasonable expectation for successfully detecting bioactive compounds.

The references do not teach the methods wherein the chromatophores of Betta. However, at the time of the claimed invention, it was well known in the art that Betta have chromatophores. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common knowledge to practice the methods of Elving and/or Lerner with a reasonable expectation for successfully detecting bioactive compounds.

The references do not teach the methods wherein the detection is computer aided. However, at the time of the claimed invention, automated (computer aided) assays were routinely employed in the art. Moreover, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use computers for support of identification/detection assays.

9. Claims 1, 3 – 4, 6 – 11, 33 – 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner in view of Kotz.

Applicant newly claims a method for detecting bioactive compounds or organisms, the method comprising providing a capsule comprising chromatophores, introducing a bioactive compound/organism into the capsule, and detecting a change in at least one chromatophore in response to the compound/organism. The chromatophores are fish; the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from a neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators, caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins; and the chromatophores are Betta chromatophores. The method further comprises exposing a first type of chromatophore to the compound, exposing a second type of chromatophore to the compound, and identifying a class of compounds based on the detected response of the chromatophores, wherein the first and second chromatophores are fish melanophores and erythrophores. The method is useful for identifying calcium channel blockers, comprising exposing an erythrophore to a compound to produce a response, exposing a melanophore to the compound to produce a response, determining if the compound has a calcium channel blocker based on the responses. The method further comprises detecting a color change from a first color prior to contact and to a second color after contact to the compound. Finally, the detection of optical change is computer aided.

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a control

compound that disperses/aggregates pigments within the melanophores; followed by exposure to the bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67). Lerner teaches that the pigment cells may be chromatophores, melanophores, or erythrophores (col.3 line 18-21) obtainable from Pisces, or fish (coll3 line 23-26).

Lerner does not specifically teach the chromatophores in capsules. However, Lerner does teach kits wherein the various components are in containers (or capsules) before use. Specifically, Lerner teaches containers with the chromatophores (col.7 – 9). Furthermore, as the references use titer wells, one of ordinary skill in the art would have known to use caps on such plates as a matter of routine aseptic laboratory practice. Thus, the capped wells would have acted as a capsule comprising chromatophores.

Lerner does not teach the method wherein both erythrophores and melanophores are used together. However, Lerner specifically teaches that melanophores and/or erythrophores may be used in the methods. At the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use either or both of the named chromatophores in the methods of Lerner with a reasonable expectation for successfully detecting bioactive compounds.

Lerner does not teach the methods wherein the chromatophores of Betta. However, at the time of the claimed invention, it was well known in the art that Betta have chromatophores. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common knowledge to practice the methods of Lerner with a reasonable expectation for successfully detecting bioactive compounds.

Lerner does not teach the method wherein both erythrophores and melanophores are used to identify calcium channel blockers. However, Kotz teaches erythrophores exhibit pigment aggregation in response to calcium influx whereas melanophores do not (abstract). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Kotz to practice the methods of Lerner in order to identify calcium channel blockers because of the known responses between the chromatophores and calcium.

The references do not teach the methods wherein the detection is computer aided. However, at the time of the claimed invention, automated (computer aided) assays were routinely employed in the art. Moreover, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use computers for support of identification/detection assays.

10. Claims 1, 3 – 9, 11, 13, 25 and 27 – 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elving and/or Lerner in view of Paul (1980).

Applicant newly claims a method for detecting bioactive compounds or organisms, the method comprising providing a capsule comprising chromatophores, introducing a bioactive compound/organism into the capsule, and detecting a change in at least one chromatophores in response to the compound/organism. The chromatophores are fish; the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from a neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators,

caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins; the organism is a bacteria, fungus, virus, plant or animal; and the chromatophores are Betta chromatophores. The method further comprises exposing a first type of chromatophore to the compound, exposing a second type of chromatophore to the compound, and identifying a class of compounds based on the detected response of the chromatophores, wherein the first and second chromatophores are fish melanophores and erythrophores. The method further comprises detecting a color change from a first color prior to contact and to a second color after contact to the compound. Alternatively, the method comprises selecting a bacteria which produces an induced response on the chromatophore, exposing the chromatophore-bacteria combination to the compound, exposing the chromatophore-cell combination to a control compound, measuring the response of the chromatophore to the control, evaluating the compound based on the cell induced response, the measured response, and the control response; wherein the test cell is a bacteria associated with a cell induced response which inhibits a chromatophore response and the control is norepinephrine. Finally, the detection of optical change is computer aided.

Elving teaches a method for detecting a pertussis toxin (bioactive compound), comprising exposing toxin sensitive fish chromatophores to a sample (compound), and observing for changes in color (abstract). Specifically, the method includes observing for pigment aggregation and hue changes (col.2 line 36-40). Fish chromatophores are exposed compounds that aggregate pigments, then to samples of body fluid (which contain bacterium) wherein the toxin inhibits pigment aggregation (or the chromatophore response), and is observed for color changes (col.2

line 36-46). Melanophores are used because they provide distinct and rapid color change (col.3 line 1-3) and noradrenaline (norepinephrine) is used as the control (col.3 line 65 – col.4 line 5).

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a control compound that disperses/aggregates pigments within the melanophores; followed by exposure to the bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67). Lerner teaches that the pigment cells may be chromatophores, melanophores, or erythrophores (col.3 line 18-21) obtainable from Pisces, or fish (coll3 line 23-26).

The references do not specifically teach the chromatophores in capsules. However, Elving and Lerner both teach kits wherein the various components are in containers (or capsules) before use. Specifically, Elving teaches separately packaged chromatophores (col.3 line 35 – 47) and Lerner teaches containers with the chromatophores (col.7 – 9). Furthermore, as the references use titer wells, one of ordinary skill in the art would have known to use caps on such plates as a matter of routine aseptic laboratory practice. Thus, the capped wells would have acted as a capsule comprising chromatophores.

The references do not teach the method wherein both erythrophores and melanophores are used together. However, Lerner specifically teaches that melanophores and/or erythrophores may be used in the methods. At the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use either or both of the named chromatophores in the methods of Lerner and/or Elving with a reasonable expectation for successfully detecting bioactive compounds.

The references do not teach the methods wherein the chromatophores of Betta. However, at the time of the claimed invention, it was well known in the art that Betta have chromatophores. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common knowledge to practice the methods of Elving and/or Lerner with a reasonable expectation for successfully detecting bioactive compounds.

The references do not teach the methods wherein the detection is computer aided. However, at the time of the claimed invention, automated (computer aided) assays were routinely employed in the art. Moreover, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use computers for support of identification/detection assays.

Finally, although the references do not teach the chromatophores in beads, glass or alginate, such entrapment was known and used in the art at the time of the claimed invention. In support, Paul teaches chromatophores that are entrapped in alginate beads (abstract). Moreover, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use chromatophores entrapped in alginate beads as a matter of routine experimentation.

Applicant argues that the references do not teach capsules containing chromatophores and that the capsulated chromatophores work unexpectedly better than those that are not. Applicant additionally argues that Elving and Lerner do not teach identification of organisms, but of compounds. Finally, Applicant argues the references do not teach betta chromatophores or using multiple classes of chromatophores.

However, these arguments fail to persuade because as stated above, the packaging of and use of titer wells with caps act to provide "a capsule comprising chromatophores", or "sealed container" comprising chromatophores. Regarding the unexpected advantages, applicant fails to provide any data or comparison suggesting these unexpected advantages.

In response to applicant's argument that the references fail to detect organisms, it is noted that the claims are drawn to detecting compounds or organisms, not only organisms. Thus the argument is not commensurate in scope with the claim. In addition, Elving teaches detecting pertussis toxin, which is indicative of the presence of an organism.

Finally, while the references do not specifically teach betta chromatophores or multiple classes of chromatophores, they do teach fish chromatophores in their methods. As stated above, it was well known in the art that Betta have chromatophores. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common knowledge to practice the methods of Elving and/or Lerner with a reasonable expectation for successfully detecting bioactive compounds. Furtermore, Lerner specifically teaches that melanophores and/or erythrophores may be used in the methods. At the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use either or both of the named chromatophores in the methods of Lerner and/or Elving with a reasonable expectation for successfully detecting bioactive compounds.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth Davis, whose telephone number is (703) 308-6310.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn, can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Effective January 20, 2004, any inquires should be made to Ruth Davis, whose telephone number is 571-272-0915. The examiner's supervisor, Michael Wityshyn, can be reached at 571-272-0926.

Ruth A. Davis; rad
December 13, 2003.

LEON B. LANKFORD, JR.
PRIMARY EXAMINER